PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Wisconsin Card Sorting Test Scores and Clinical and Socio-demographic Correlates in Schizophrenia: Multiple Logistic Regression Analysis
AUTHORS	Okada, Takashi; Banno, Masahiro; Koide, Takayoshi; Aleksic, Branko; Kikuchi, Tsutomu; Kohmura, Kunihiro; Adachi, Yasunori; Kawano, Naoko; Iidaka, Tetsuya; Ozaki, Norio

VERSION 1 - REVIEW

REVIEWER	Kao Chin Chen M.D. Lecturer, Department of Psychiatry, College of Medicine National Cheng Kung University 138, Sheng-Li Road, Tainan 70428, Taiwan
REVIEW RETURNED	11-Jun-2012

GENERAL COMMENTS	RE: bmjopen-2012-001340, Wisconsin Card Sorting Test Scores and Relevant Clinical Factors in Schizophrenia: Multiple Logistic Regression Analysis This study tried to investigate the relationship between factors derived from Wisconsin Card Sorting Test (WCST) and clinical demographic data of Japanese patients with schizophrenia. Although authors emphasize the interesting concept of WCST factors and suggest the demographic data of patients could affect the WCST factors. There are several major points need to be considered further as below, 1. In general, this manuscript still needs an English proof reading in order to correct some grammatical errors and help readers to understand authors' messages better. 2. Abstract, A、 Please revise the term "schizophrenic patients" into "patients with schizophrenia". Results, page 4, line 6-8, "We assessed relationship between these factor scores and clinical factors, using multiple logistic regression analysis." should be moved into the previous part , Primary and secondary outcome measures: . 3. Introduction, A、 It should focus more on the key issues that authors wish to investigate and avoid unnecessary information in order to clearly show the main aims of this study, for example, IQ related information may not be necessary. B、 The 1st paragraph (Page 6, Line 12-19, 19-25) and 2nd paragraph shall have references added. The 2nd paragraph, page 6, line 34, please clarify the meaning of "pattern of intelligence". C、 Page 6, line 56 and page 7, line 6-10, this paragraph sounded

	odd. Page 7, line 27-29, a reference may be necessary to support this statement. 4. Methods and procedures, A、 The recruitment of participants, authors shall mention from which department in 3 hospitals the recruitment took place, the outpatient department or the acute or/chronic ward? Since the relation between the severity of psychotic symptoms and WCST was investigated later in this study. Is there any concordant medication used by patients in spite of antipsychotics, such as anxiolytics, BZD etc. (Table 1, polytherapy)? The WCST assessment procedure, who performed the assessment? B、 Page8, line 56, “Recruitment for the participants occurred between July 2009 and August 2011. “would be better to revised into “ Participants were recruited from July 2009 to August 2011.” C、 Page 9, line 14 “included” shall be “recruited”; line 30, why did authors mention “ ….and self-identified as Japanese.” about the subjects? Please clarify this statement. D、 Page 11, line 10-12, please clarify this statement: “Sex was categorized in terms of biology and was self-reported by the schizophrenic patients.” 5. Statistical analysis, A、 The rationale and methodology (i.e. Kaiser's criteria and unrotated solution) of applying principle component analysis as a mean of data reduction are appropriate. However, to dichotomize the continuous factor scores by using the median as a cutoff point for logistic regression may be unjustified yet. What were the scores of factors referred to? Furthermore, for logistic regression analysis, the authors converted factor scores into categorical variables by using the median as a cutoff point, is there any reference to support this method? No strong rationale (e.g. for moderator analysis, for risk factor analysis between case and non-case) could be found to use logistic regression in this study yet. A series of multiple linear regressions as the main analysis would be better suitable. 6. Results A、 The effect of duration of illness on one factor of WCST (i.e. factor 2 was influenced by DMS) is the novel finding of this study, table 4. However, another analysis (table S4) also showed that DMS is not significantly associated with the duration of illness. This discrepancy between the Main analysis and Sub-analysis should be explained carefully in order to conclude this novel finding. B、 Table 1, the subtypes of schizophrenia and even the variety of antipsychotics could be deleted since they were not applied in the analyses. 7. Discussion and Limitations A、 Page 17, the 2nd and 3rd paragraphs need to be revised in order to help readers to understand better. B、 Sub-analysis, page 17, line 54 and page 18, 1st paragraph need to be revised in order to help readers to understand better. C、 The Chlorpromazine equivalent doses did not affect the WCST and the different effects of PANSS (positive, negative) toward WCST should be mentioned and interpreted. 8. Conclusion A、 The significant interaction between the duration of illness and a factor of WCST could not be concluded yet and it needs further

	confirmation.

REVIEWER	Hmed Rady, MD Senior lecturer of Neuropsychiatry Alexandria University School of Medicine P.O.BOX 518 Alexandria 21511 Egypt
REVIEW RETURNED	31-Jul-2012

THE STUDY	the english language used in the manuscript is very poor and hard to follow, the title of the manuscript is not really reflecting what authors found. it's not only about clinicatl factors in schizophrenia but also sociodemographic factors and I would suggest to use ' clinical and socio demographic correlates in schizophrenia ' instead of ' factors ' it has been mentioned several times the word ' WCST characteristics ' though different subcategories measured by WCST are better described as ' WCST parameters or items '
RESULTS & CONCLUSIONS	Though results are interseting, and to my knowledge it's the first time to correlate different demographic parameters to performance on WCST whech render such research work innovative. but authors did not provide an explanation of their own to findings, of particular interest the poor performance that was correlated to score on the negative subscale of the PANSS a finding that contradicts many authors supporting the idea that cognitive impairment is not correlated to negative or positive subscales of PANSS and should be considered a separate entity. the phrase in conclusion section ' WCST facor scores may be useful may be useful to assess cognitive impairment in schizophrenic patients using WCST while avoiding problems from multiple comparisons ' is ambigous and I cannot understand what authors are trying to highlight !

VERSION 1 – AUTHOR RESPONSE

Responses to Reviewer #1

We are grateful to reviewer #1 for the critical comments and useful suggestions that have helped us to considerably improve our manuscript. As indicated in the responses that follow, we have taken all of these comments and suggestions into account in the revised version of our manuscript.

1. In general, this manuscript still needs an English proof reading in order to correct some grammatical errors and help readers to understand authors' messages better.

Thank you very much for your comments. We took advantage of professional English proofreading to correct grammatical errors and help readers to understand our messages better before we submitted the original manuscript and revised manuscript.

2. Abstract

A. Please revise the term "schizophrenic patients" into "patients with schizophrenia". Results, page 4, line 6-8, "We assessed relationship between these factor scores and clinical factors, using multiple logistic regression analysis." should be moved into the previous part, Primary and secondary outcome measures.

Thank you very much for your comments. We revised the term “schizophrenic patients” as “patients with schizophrenia” in manuscript, figures and tables.
We moved “From the principal component analysis, we identified two factors (1 and 2). We assessed the relationship between these factor scores and clinical and socio-demographic factors, using multiple logistic regression analysis.” into Primary and secondary outcome measures.

3. Introduction
A. It should focus more on the key issues that authors wish to investigate and avoid unnecessary information in order to clearly show the main aims of this study, for example, IQ related information may not be necessary.

Thank you very much for your comment. According to the reviewer’s suggestion, we have shortened the introduction section by deleting some of the IQ related information.

B. The 1st paragraph (Page 6, Line 12-19, 19-25) and 2nd paragraph shall have references added. The 2nd paragraph, page 6, line 34, please clarify the meaning of “pattern of intelligence”.

Thank you very much for your comment. We added references to the 1st paragraph (Page 6, Line 4-8, 8-10) and 2nd paragraph.
We revised Page 6, Line 8-10 and Line 15-17 considering the contents of the references.

Revised manuscript (Page 6, Line 8-10): Introduction

“Many studies using brain imaging suggest that neurobiological changes in the brain are related to the cognitive impairment in schizophrenia.”

Revised manuscript (Page 6, Line 15-17): Introduction

“Second, intelligence level, intelligence profile (verbal IQ and performance IQ), and educational level could affect cognitive impairment in patients with schizophrenia.”

Page 6, Line 15, “pattern of intelligence” meant intelligence profile (verbal IQ and performance IQ). Therefore, we revised the manuscript as follows.

Revised manuscript (Page 6, Line 15-16): Introduction

“intelligence profile (verbal IQ and performance IQ)”

C. Page 6, line 56 and page 7, line 6-10, this paragraph sounded odd. Page 7, line 27-29, a reference may be necessary to support this statement.

Thank you very much for your comment. We removed the unnecessary sentence “Therefore, we investigated the relationship between WCST scores and clinical factors in this study.” from the paragraph. We also added references to Page 7, Line 11-12.

4. Methods and procedures
A. The recruitment of participants, authors shall mention from which department in 3 hospitals the

recruitment took place, the outpatient department or the acute or/chronic ward? Since the relation between the severity of psychotic symptoms and WCST was investigated later in this study. Is there any concordant medication used by patients in spite of antipsychotics, such as anxiolytics, BZD etc. (Table 1, polytherapy)? The WCST assessment procedure, who performed the assessment?

Thank you very much for your comments. The recruitment took place from both the outpatient department and the acute / chronic wards in three hospitals. 51 outpatients (15 acute phase patients and 36 chronic phase patients) and 55 inpatients (37 acute phase patients and 18 chronic phase patients) were recruited. 25 patients were unspecified (outpatients or inpatients: 20 acute phase patients and 5 chronic phase patients). We did not select outpatients / inpatients as an independent variable in main and sub-analysis, because we could not obtain the information about outpatients / inpatients in 19% of the subjects. We revised manuscript as follows.

Revised manuscript (Page 8, Line 24-Page 9, Line 4): Methods and procedures

“The recruitment took place from both the outpatient department and the acute / chronic wards in three hospitals. 51 outpatients (15 acute phase patients and 36 chronic phase patients) and 55 inpatients (37 acute phase patients and 18 chronic phase patients) were recruited. 25 patients were unspecified (outpatients or inpatients: 20 acute phase patients and 5 chronic phase patients).”

104 patients (78%) were receiving concomitant medications including benzodiazepines, barbiturates, anticholinergics, mood stabilizers, and antidepressants. Polytherapy in Table 1 meant therapy using two or more antipsychotics. We revised the manuscript as follows.

Revised manuscript (Page 9, Line 6-8): Methods and procedures

“104 patients (78%) were receiving concomitant medications, which could include benzodiazepines, barbiturates, anticholinergics, mood stabilizers, and antidepressants.”

Psychiatrists in three hospitals performed the assessment. We revised manuscript as follows.

Revised manuscript (Page 11, Line 4-5): Methods and procedures

“Psychiatrists in three hospitals performed the KWCST assessment.”

B. Page8, line 56, “Recruitment for the participants occurred between July 2009 and August 2011. “would be better to revised into “ Participants were recruited from July 2009 to August 2011.”

Thank you very much for your comments. We revised Page 9, Line 4-5 according to the reviewer’s suggestion.

Revised manuscript (Page 9, Line 4-5): Methods and procedures

“Participants were recruited from July 2009 to August 2011.”

C. Page 9, line 14 “included” shall be “recruited”; line 30, why did authors mention “ ….and self-identified as Japanese.” about the subjects? Please clarify this statement.

Thank you very much for your comments. We revised Page 9, Line 12 from “included” to “recruited”. “and self-identified as Japanese” meant we recruited Japanese patients. We removed this part in

order to help readers to understand better.

D. Page 11, line 10-12, please clarify this statement: “Sex was categorized in terms of biology and was self-reported by the schizophrenic patients.”

Thank you very much for your comments. “Sex was categorized in terms of biology and was self-reported by the schizophrenic patients.” meant we determined the sex of participants according to their self-reports. We revised Page 11, Line 10 as follows.

Revised manuscript (Page 11, Line 10): Methods and procedures

“Sex was determined by patients’ self-reports.”

5. Statistical analysis
A. The rationale and methodology (i.e. Kaiser's criteria and unrotated solution) of applying principle component analysis as a mean of data reduction are appropriate. However, to dichotomize the continuous factor scores by using the median as a cutoff point for logistic regression may be unjustified yet. What were the scores of factors referred to? Furthermore, for logistic regression analysis, the authors converted factor scores into categorical variables by using the median as a cutoff point, is there any reference to support this method? No strong rationale (e.g. for moderator analysis, for risk factor analysis between case and non-case) could be found to use logistic regression in this study yet. A series of multiple linear regressions as the main analysis would be better suitable.

Thank you very much for your comments. The reason we adopted the multiple logistic regression was the distribution of dependent variables (WCST factor scores). To conduct multiple linear regression analysis, normality of dependent variables is needed. (Osborne JW, Waters E. Four Assumptions Of Multiple Regression That Researchers Should Always Test. Practical Assessment, Research, and Evaluation 2002;8:1-9.) About the distribution of dependent variables (WCST factor scores) in this study, P-values of two kinds of normality test (Kolmogorov-Smirnov test and Shapiro-Wilk test) were less than 0.001. We also tested normality of the logarithmic distribution of dependent variables (WCST factor scores), and the P-values of two kinds of normality test (Kolmogorov-Smirnov test and Shapiro-Wilk test) were less than 0.001. Multiple logistic regression can analyze variables in non-normality. (Peng CYJ, Lee KL, Ingersoll GM. An introduction to logistic regression analysis and reporting. J Educ Res 2002;96:3-14.)
We added a supplementary file, Information S1 (Web only file), to explain why we did not use multiple linear regression analysis.

We converted factor scores into categorical variables for multiple logistic regression analysis because dependent variables in multiple logistic regression analysis should be binary values. There were two reasons that we used the median as a cutoff point for the dependent variables (WCST factor scores) in the multiple logistic regression analysis. First, one previous psychiatric research study used the median as a cutoff point in dependent variables of multiple logistic regression analysis. (Jackson CT, Fein D, Essock SM, Mueser KT. The effects of cognitive impairment and substance abuse on psychiatric hospitalizations. Community Ment Health J 2001;37:303-12.) Second, the most common approach was to take the sample median in dichotomizing continuous variables because there were no cutoff points of WCST factor scores in previous studies. (Altman DG, Royston P. The cost of dichotomising continuous variables. BMJ 2006;332:1080.)
We provided a supplementary file, Information S2 (Web only file) in order to explain the reason we used the median as a cutoff point for the dependent variables (WCST factor scores) in the multiple logistic regression analysis.

We also added a statement about the limitations of dichotomizing continuous variables (WCST factor scores).

Revised manuscript (Page 19, Line 21-24): Discussion

“Third, we dichotomized continuous variables (WCST factor scores) in the multiple logistic regression analysis. Therefore, careful interpretation of the results may be needed, considering the statistical weak points of dichotomizing continuous variables. (Altman DG, Royston P. The cost of dichotomising continuous variables. BMJ 2006;332:1080.)”

6. Results
A. The effect of duration of illness on one factor of WCST (i.e. factor 2 was influenced by DMS) is the novel finding of this study, table 4. However, another analysis (table S4) also showed that DMS is not significantly associated with the duration of illness. This discrepancy between the Main analysis and Sub-analysis should be explained carefully in order to conclude this novel finding.

Thank you very much for your comments. The effect of duration of illness on WCST factor 2 score (i.e. factor 2 was mainly influenced by DMS) is the novel finding in main analysis. However, DMS is not significantly associated with the duration of illness in sub-analysis (Table S4 (Web only file)). This discrepancy between the main analysis and sub-analysis may be derived from the difference between DMS and factor 2 (Factor 2 included not only the DMS, but also CA, PEM, PEN and TE). We added this discussion to our manuscript as follows.

Revised manuscript (Page 19, Line 1-6): Discussion

“The effect of duration of illness on WCST factor 2 score, which was mainly influenced by DMS, is the novel finding of the main analysis. However, DMS is not significantly associated with the duration of illness in the sub-analysis (Table S4 (Web only file)). This discrepancy between the main analysis and sub-analysis may be derived from the difference between DMS and factor 2 (Factor 2 included not only DMS, but also CA, PEM, PEN and TE).”

B. Table 1, the subtypes of schizophrenia and even the variety of antipsychotics could be deleted since they were not applied in the analyses.

Thank you very much for your comments. We deleted the subtypes of schizophrenia and the variety of antipsychotics in Table 1.

7. Discussion and Limitations
A. Page 17, the 2nd and 3rd paragraphs need to be revised in order to help readers to understand better.

Thank you very much for your comments. We revised these paragraphs, Table 4 and Table S3 in order to help readers to understand better.

Revised manuscript (Page 17, Line 22-Page 18, Line 7): Discussion

“The shared findings were that age and PANSS negative scale score were related to WCST scores (Table 4).[9 10 23]

Two findings differed from previous studies (Table 4).[9 10 23] First, we found a new relationship between education years and WCST scores. Second, we found no relationship between age of onset and WCST scores. Differences in the results between previous studies [9 10 23] and our study may be explained by differences of ethnicity, distribution of age and education years, types of statistical analysis used, and the version of WCST. These differences suggest that future studies about WCST should be conducted with attention to these conditions."

B. Sub-analysis, page 17, line 54 and page 18, 1st paragraph need to be revised in order to help readers to understand better.

Thank you for pointing this out. We revised the manuscript as follows.

Revised manuscript (Page 18, Line 22-24): Discussion

"We found that factor 1 score and factor 1 score's main components (CA, PEM, PEN and TE) related to age and education years (Table S4 (Web only file))."

C. The Chlorpromazine equivalent doses did not affect the WCST and the different effects of PANSS (positive, negative) toward WCST should be mentioned and interpreted.

In the revised manuscript, we mentioned and interpret this result.

Revised manuscript (Page 15, Line 10-12): Results

"CPZ equivalent doses did not affect the WCST scores. PANSS positive scale score did not affect the WCST scores; whereas PANSS negative scale score did."

Revised manuscript (Page 18, Line 8-18): Discussion

"CPZ equivalent doses did not affect the WCST scores in this study. This result was in the same direction as one meta-analysis (n=4524) though recent studies had suggested the possibility of an effect.[31 39 40] Future studies will be necessary to clarify whether CPZ equivalent doses affect WCST scores under other conditions.
PANSS positive scale score did not affect the WCST scores but the PANSS negative scale score did. A recent meta-analysis (n=6519) suggested that negative symptoms related to cognitive performance in patients with schizophrenia whereas positive symptoms did not.[41] This suggests that the relationships between PANSS positive and negative scale scores and WCST scores in this study may be reasonable."

8. Conclusion
A. The significant interaction between the duration of illness and a factor of WCST could not be concluded yet and it needs further confirmation.

Thank you very much for your comments. We agree that this needs further confirmation in future studies because of the discrepancy between the results of main analysis and sub-analysis in this study. We revised the manuscript as follows.

Revised manuscript (Page 20, Line 10-13): Conclusion

“The interaction between the duration of illness and a factor of the WCST needs further confirmation in future studies because there was a discrepancy between the results of the main analysis and the sub-analysis in this study.”

Responses to Reviewer #2

We would like to express our gratitude to the reviewer #2 for the critical comments and useful suggestions that have helped us to considerably improve our manuscript. As indicated in the responses that follow, we have taken all these comments and suggestions into account in the revised version of our manuscript.

1. The English language used in the manuscript is very poor and hard to follow, the title of the manuscript is not really reflecting what authors found. It's not only about clinical factors in schizophrenia but also sociodemographic factors and I would suggest to use ' clinical and socio demographic correlates in schizophrenia ' instead of ' factors '
It has been mentioned several times the word ' WCST characteristics ' though different subcategories measured by WCST are better described as ' WCST parameters or items '

Thank you very much for your comments. We took advantage of professional English proofreading to correct grammatical errors and help readers to understand our message better before we submitted the original manuscript and revised manuscript.
We changed the title of the manuscript following the reviewer’s suggestion. The new title was “Wisconsin Card Sorting Test Scores and Clinical and Socio-demographic Correlates in Schizophrenia: Multiple Logistic Regression Analysis”. We changed the term ‘clinical factors’ to ‘clinical and socio-demographic factors’ in the manuscript, figures and tables.
We changed the term ‘WCST characteristics’ to ‘WCST parameters or items’.

2. Though results are interesting, and to my knowledge it's the first time to correlate different demographic parameters to performance on WCST, which render such research work innovative. But authors did not provide an explanation of their own to findings, of particular interest the poor performance that was correlated to score on the negative subscale of the PANSS a finding that contradicts many authors supporting the idea that cognitive impairment is not correlated to negative or positive subscales of PANSS and should be considered a separate entity.

Thank you very much for your comments. We discussed and provided an explanation about the relationship between PANSS positive and negative scale scores and cognitive performance in patients with schizophrenia.

Revised manuscript (Page 18, Line 13-18): Discussion

“PANSS positive scale score did not affect the WCST scores but the PANSS negative scale score did. A recent meta-analysis (n=6519) suggested that negative symptoms related to cognitive performance in patients with schizophrenia whereas positive symptoms did not.[41] This suggests that the relationships between PANSS positive and negative scale scores and WCST scores in this study may be reasonable.”

3. The phrase in conclusion section ' WCST factor scores may be useful to assess cognitive impairment in schizophrenic patients using WCST while avoiding problems from multiple comparisons

' is ambiguous and I cannot understand what authors are trying to highlight !

Thank you very much for your comments. We revised the sentence in order to help readers to understand better.

Revised manuscript (Page 4, Line 7-9): Conclusions in Abstract

“Using WCST factor scores may reduce the possibility of type I errors due to multiple comparisons.”

Revised manuscript (Page 5, Line 13-14): Key messages

“Using WCST factor scores may reduce the possibility of type I errors due to multiple comparisons.”

Revised manuscript (Page 16, Line 8-10): Discussion

“In assessment of cognitive function in patients with schizophrenia, using the WCST factor scores may reduce the possibility of type I errors due to multiple comparisons.”

Revised manuscript (Page 17, Line 8-10): Discussion

“WCST factor scores calculated by principal component analysis may be useful for reducing the possibility of type I errors due to multiple comparisons.”

VERSION 2 – REVIEW

REVIEWER	Kao Chin Chen M.D. Lecturer, Department of Psychiatry, College of Medicine National Cheng Kung University 138, Sheng-Li Road, Tainan 70428, Taiwan
REVIEW RETURNED	27-Sep-2012

THE STUDY	This manuscript has been extensively revised. The authors have particularly provided the information which justifies the dichotomized data analyses (violation of normal distribution), and addressed the potential problem in the conclusion. I only have few minor comments: 1. Measurement Settings, Clinical and socio-demographic factors, “Sex was determined by patients’ self-reports.” (Page 11, line 10), this statement should be deleted to avoid readers’ confusion. 2. I am not sure that whether the principal component analysis (PCA) model here is all based on Spearman correlation matrix. I would suggest the authors to recheck it since the input of the Spearman correlation matrix in Table 2 did not show the same result in Table 3.
RESULTS & CONCLUSIONS	This manuscript has been extensively revised. The authors have particularly provided the information which justifies the dichotomized data analyses (violation of normal distribution), and addressed the potential problem in the conclusion. I only have few minor comments: 1. Measurement Settings, Clinical and socio-demographic factors, “Sex was determined by patients’ self-reports.” (Page 11, line 10),

	this statement should be deleted to avoid readers' confusion. 2. I am not sure that whether the principal component analysis (PCA) model here is all based on Spearman correlation matrix. I would suggest the authors to recheck it since the input of the Spearman correlation matrix in Table 2 did not show the same result in Table 3.

VERSION 2 – AUTHOR RESPONSE

Responses to Reviewer #1

We are grateful to reviewer #1 for the critical comments and useful suggestions that have helped us to considerably improve our manuscript. As indicated in the responses that follow, we have taken all of these comments and suggestions into account in the revised version of our manuscript.

1. Measurement Settings, Clinical and socio-demographic factors, "Sex was determined by patients' self-reports." (Page 11, line 10), this statement should be deleted to avoid readers' confusion.

Thank you very much for your comments. We deleted the statement "Sex was determined by patients' self-reports." in order to avoid reader's confusion.

2. I am not sure that whether the principal component analysis (PCA) model here is all based on Spearman correlation matrix. I would suggest the authors to recheck it since the input of the Spearman correlation matrix in Table 2 did not show the same result in Table 3.

Thank you very much for your comments. The difference between results is related to the statistical methods. In other words, the principal component model (Table 3) was based on Pearson's correlation matrix and not on the Spearman's correlation matrix. We added the Pearson's product moment correlation coefficients as Table S1. Furthermore, in order to avoid misinterpretations, we revised manuscript as below:

Revised manuscript (Page 12, Line 7-9): Methods and procedures

"The principal component model was based on Pearson's correlation matrix. We showed the Pearson's product moment correlation coefficients between the five indicators of WCST in Table S1 (Web only file)."

Revised manuscript (Page 17, Line 15-21): Discussion

"We compared the Spearman's rank correlation coefficients with the Pearson's product moment correlation coefficients between the five indicators of WCST (Table 2 and Table S1). Correlations between CA, PEM, PEN and TE and a correlation between CA and DMS were statistically significant ($P<0.001$). In this point, both correlation coefficients showed the same direction. Therefore, using Pearson's correlation matrix, instead of Spearman's correlation matrix, in principal component analysis may be justified in our study."

Revised manuscript (Page 20, Line 5-8): Discussion

"Third, instead of using Spearman's correlation matrix in the principal component analysis, which might be more appropriate method in terms of the non-normal distribution of five

WCST indicators, we used Pearson’s correlation matrix.”